

3. Laubischer: Virchow's Arch. of Path. Anat., 104:434, 1886.
4. Meltzer and Auer: Am. J. Physiol., 14:366, 1906; 15:387, 1906.
5. Matthews, S. A., and Jackson, D. E.: Am. J. Physiol., 19:5 (June), 1907.
6. Lazard, E. M.: Am. J. Obst. and Gynec. (June), 1927.
7. Wegener, Henry P.: Ann. Int. Med., p. 222 (Sept.), 1930.
8. Osler: Practice of Medicine, 6:182-183.

DISCUSSION

E. M. LAZARD, M. D. (1930 Wilshire Boulevard, Los Angeles).—The author's experience with the intravenous use of magnesium sulphate in hypertension and allied eye conditions is of much interest to those of us who have been so greatly impressed with its value in the preclampsic toxemias and eclampsics for the past ten years. The clinical results reported by Doctor Lissner, viz., control of muscular twitching, relief of headache, and of epigastric distress (all of which, in the pregnant woman, are premonitory signs of an impending eclamptic attack), serve to confirm the results which we have had with the intravenous magnesium sulphate treatment of eclampsia and pre-eclamptic toxemia.

That the author has not observed the diuretic effect, and the comparatively rapid reduction of the edema, which we have obtained in the eclampsics, is due, I believe, rather to the small doses of the salt that he uses than to the difference in the underlying kidney pathology. His regular dosage is 10 cubic centimeters of a 10 per cent solution, not oftener than once daily, whereas our standard dosage is 20 cubic centimeters of a 10 per cent solution repeated, as necessary for the control of symptoms, frequently, twelve or fourteen such injections being given in twenty-four hours.

That these results have been obtained in such chronic conditions as essential hypertension and chronic nephritis, further justifies its use in the eclamptic syndrome which so closely resembles the clinical picture in these nonpregnant individuals, even though the etiologic factors in the various types of the eclamptic toxemia are so different.

I can also confirm the last conclusion in Doctor Lissner's paper that "there are no untoward symptoms from frequent injections of controlled amounts of magnesium sulphate intravenously." In many thousand injections of magnesium sulphate in the eclamptic toxemias, we have never observed any bad effects that could be attributed to injections in the proper dosage.

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HYMAN RAPAPORT, M. D. (1048 Temple Street, Los Angeles).—About three years ago, after learning of Doctor Lissner's favorable results, I began to use magnesium sulphate intravenously in hypertension. I limited its use to those hypertensives whose outstanding complaints were dizziness, severe throbbing headaches, and extreme irritability. The usual dose given was 10 cubic centimeters of a 10 per cent solution daily.

The results were gratifying. There were no toxic reactions, but there were some complaints of a feeling of warmth following the injection. This discomfort was greatly alleviated by injecting the solution very slowly. The injections invariably relieved the dizziness, headache, and irritability, some of the patients having markedly improved after the first administration. It was notable that the relief of the symptoms was out of proportion to the drop in the blood pressure.

The irritability in hypertensives is apparently due to an overstimulation of the nervous motor mechanism; and since this is the point depressed by the magnesium, hence the relief of the irritability. Doctor Lissner's observations on the reduction of intra-ocular tension are interesting, and should stimulate further clinical study. From my personal experience with the use of the magnesium sulphate intravenously in hypertension, I am convinced that it occupies a definite place in the armamentarium of the therapeutics of hypertension.

GABRIEL SEGALL, M. D. (1930 Wilshire Boulevard, Los Angeles).—Any medication or drug which may influence the course of hypertension beneficially, or alleviate the symptom-complex of hypertension, should be given serious consideration.

Doctor Lissner's study and experience with magnesium sulphate must be considered an advance in the approach of coping with the therapeutic problem of hypertension. Inasmuch as the state of hypertension has a variety of etiologic factors, it is natural that there cannot be one type of medication suitable to all forms of the condition. However, we know that, no matter what the etiology in such cases is, there are two main factors involved: hypertonus of the arterial wall of the vessels and angiospasm. Even if there is no atheromatosis primarily present, both of those factors may lead to degeneration of the intima of the vessels, and eventually to systemic hypertension. It has also been my experience that magnesium sulphate, used according to the method and technique of Doctor Lissner, has an excellent effect upon the reduction of hypertension and its secondary symptoms. The mode of action is difficult to determine; the quantity of magnesium sulphate used could hardly be considered sufficient to exercise such a sedative and hypotensive action. The results of magnesium sulphate in uremia and preuremic conditions may lead one to the assumption that magnesium sulphate acts against edema of the brain. It probably relaxes the vascular spasms by direct action on the vasomotor center of the medulla. I have never observed any discomfort or untoward effects in any of my patients treated with this method.

Therefore, there being no contraindications present for the use of an apparently helpful and harmless drug, it would seem that this method advocated by Doctor Lissner should be applied in the treatment of hypertension.

CHOLECYSTIC DISEASE IN PIGS, SHEEP AND CATTLE*

By STANLEY H. MENTZER, M. D.
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IN a previous study I called attention to the incidence of cholecystic disease in pigs, sheep, and cattle slaughtered in an abattoir in St. Paul, Minnesota. My present study was conducted in San Francisco and repeated because of an opportunity to segregate the pigs according to their food supply. Studies of the incidence of gall-stones in man, in varying geographic areas, seem to indicate that food plays a significant part in the etiology of gall-stones. Hence, the privilege to observe controlled food sources in animals in relation to the incidence of gall-stone formation appeared opportune.

MATERIAL FOR THE STUDY

The pigs arrived in the abattoir in groups and were kept separate during their preparation, so that we might adequately study the effect of grain and swill feeding in relation to cholecystic disease. There were 712 grain-fed and 252 swill-fed hogs. Gall-stones were found in seven, an incidence of 0.72 per cent. Approximately 60 per cent of the stones occurred in the swill-fed group, data which proved surprising, for we expected that the incidence in the swill-fed hogs would be much

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Note.—This article from a member of the California Medical Association has been accepted in order that these studies shall find a place in the medical literature. The value of the work lies in its application to medicine, because the data contained therein is to be used as the basis for future comparative studies.

greater. However, three of the swill-fed pigs had cholesterol stones in their gall-bladders, while four animals had bilirubin calcium stones, all of which came from grain-fed hogs. Obviously, food seemed an important factor in relation to the type of stone formed. Its significance is lessened, however, when we recall that Gauss and Davis found cholesterol-rich stones in twenty-one of 2,067 cattle (1 per cent). Cattle are not fed fat-containing foods, yet all of the stones in Gauss and Davis' cases were fat stones. In my previous study I found that 0.8 per cent of five thousand cattle had gall-stones, but the majority of stones from the gall-bladders of cattle in that study were bilirubin calcium stones. Totten found calculi in twenty-three of 5,725 cattle (0.4 per cent) in a Minnesota abattoir, but he did not specify the type of gall-stone encountered. In my previous study, 8 per cent of the pigs had gall-stones while only 0.72 per cent of the present group had them. The explanation of this apparent discrepancy was evident when the sex and pregnancy factors were studied, however. Sows predominated in my St. Paul study. Only 20 per cent of the pigs slaughtered in the San Francisco abattoir were females. I had believed that the type of food was the most important single factor in gall-stone formation, but these data seemed to show that sex, and particularly pregnancy, were of greater significance. Pregnancy was the most important factor in association with gall-stone disease in cattle also, as Gauss and Davis' statistics showed. They found biliary calculi in twenty-one of 2,067 cattle; of these, seventeen occurred in adult cows that had calved and eight were pregnant at the time. Heifers (adolescent females) comprised the greatest number of cattle slaughtered, yet no stones were found in them. However, sex and pregnancy are not wholly important, for biliary calculi were found in 1.2 per cent of the bulls and 1.0 per cent of the steers in comparison with 2.3 per cent of the cows.

Four hundred adult sheep's gall-bladders were examined in the present study and calculi found in seven, an incidence of 1.75 per cent. With one exception all of the stones were small, spiculed bilirubin calcium stones, and usually only one stone was found in a specimen. One hundred gall-bladders from lambs, less than eight months old, were also examined, but none contained biliary calculi or other pathology.

Thirty-seven cows and forty-six steers were also investigated, but no stones were found in the gall-bladders of any of these animals. Only a small number of cattle were studied in this series, for a very large group were included in my previous work. The majority of stones in the former group were bilirubin calcium stones which were found almost entirely within the gall-bladder cavity. In Gauss and Davis' study of cattle gall-bladders, stones were found in seventeen instances, and in four additional cases they were recovered from the bile ducts. All of the stones in their series were apparently cholesterol stones.

Of greater interest and surprise was the large number of instances of cholesterosis of the gall-

bladder found in pigs and sheep (Fig. 1). I was astonished to find grossly visible lipoid (cholesterosis) in 213 of the 964 pigs (22.1 per cent). It was also surprising to note that cholesterosis occurred as frequently in the grain-fed as in the swill-fed hogs. The significant fact lay in the observation that almost all of the gall-bladders showing cholesterosis were found in hogs that had been pregnant, usually many times. Five instances of cholesterosis were found among the four hundred adult sheep's gall-bladders, while none was encountered among the lambs. Unfortunately no record was available of the pregnancy factor in the sheep. And, to disturb my thesis most, no instances of cholesterosis were found among the thirty-seven cows' gall-bladders, while two were recovered from the group of forty-six steers. Whatever preconceived notions I may have entertained relative to food or pregnancy factors as etiologic agents of cholesterosis in domestic animals, were rudely shattered by these facts. That there is some association of importance is evident, however, by the frequency of cholelithic disease in fat-fed and pregnant animals. Of the two associated factors, pregnancy seems to be the more important. It cannot be overemphasized, however, because of the finding of cholesterosis specimens in the gall-bladders of steers.

MICROSCOPIC FINDINGS

Microscopically, the cholesterosis specimens were identical with those from human cases. The fat droplets were found mainly at the bases of the epithelial cells, equally distributed above and below the nuclei, but closely grouped about them. Advanced lesions were also identical with slides from human cases, for the Sudan-stained lipoid particles were seen in the stroma as well as in the epithelial cells of the gall-bladder wall. One of the most interesting lesions found in the gall-bladder, and limited wholly to pigs, was the accumulation of lymphocytes resembling lymph nodes. Grossly these appeared as large, submucosal swellings, resembling papillomata of the human gall-bladder (Fig. 2). When I first saw these nodules I thought they were papillomata, yet they were relatively flat and sessile, never pedunculated (Fig. 3). They appeared to be possible tubercles, but microscopic sections proved them to be accumulations of lymphocytes, almost typical of lymph-node structure (Fig. 4). They were found in thirty-nine of the 964 pigs' gall-bladders (0.4 per cent). The normal pig's gall-bladder did not contain such areas, and I am unable to account for their significance. The gall-bladders in which they were found were otherwise normal except for one specimen, which contained a single bilirubin-calcium stone. Gauss and Davis reported "papillomatous nodules in the mucosa" of five cattle. No further description of them is given. It would be interesting to know if they resembled the lymphoid structures which I found in the pig's gall-bladder, and which I believed, on gross examination, to be papillomata. No such lesions were seen in the eighty-three cattle examined in my present study.

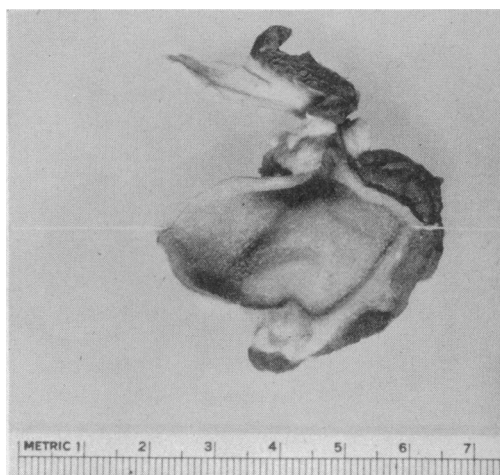


Fig. 1.—Cholesterosis, grade 2, in a sheep's gall-bladder.

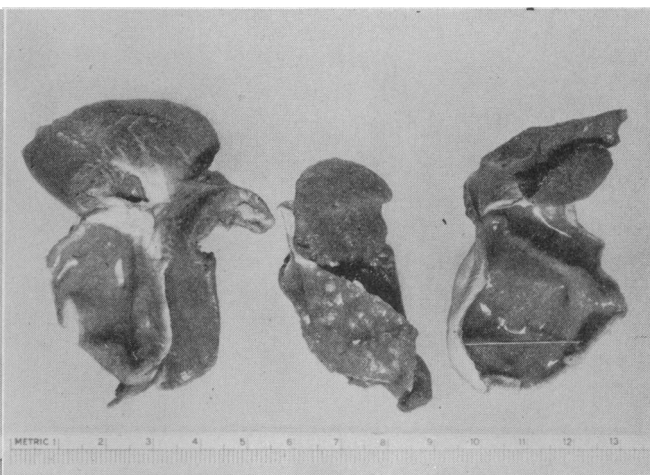


Fig. 2.—Submucosal lymphoid structures in pigs' gall-bladders.

OTHER PATHOLOGY

Acute or subacute cholecystitis, manifested by a reddened, thickened and edematous gall-bladder wall, was found in three of the 964 pigs' gall-bladders, sixteen of the 500 sheep, and one of

the typical picture of acute inflammation with congestion, hemorrhage, edema and lymphocytic or leukocytic infiltration. Chronic cholecystic disease had resulted in the deposition of calcareous material in one gall-bladder in which the wall was

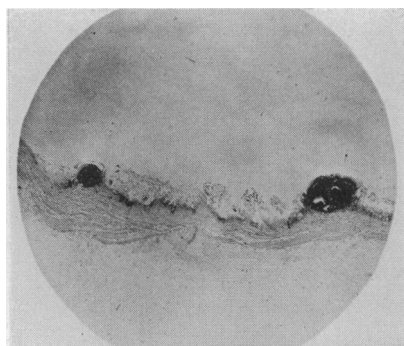


Fig. 3.—The sessile nature of the lymphoid structures is evident.

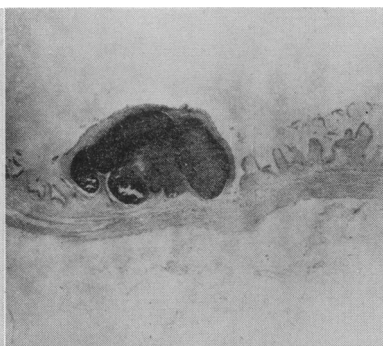


Fig. 4.—High magnification showing the lymph node structure.

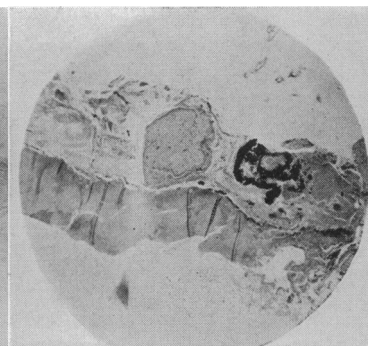


Fig. 5.—Calcareous deposit in chronic cholecystitis (pig's gall-bladder).

the eighty-three cattle. In most instances the acute inflammatory lesion was localized in the fundus or the neck of the gall-bladder, and usually not more than a third of the gall-bladder was involved. Microscopically, the gall-bladder wall presented

greatly thickened and edematous, and showed markedly hypertrophied smooth muscle bundles (Fig. 5).

One instance of duplication of the gall-bladder was found in the entire series. This specimen was

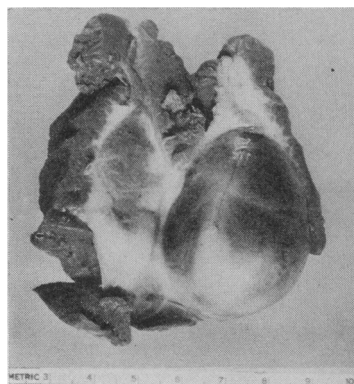


Fig. 6.—Double gall-bladder in a pig.

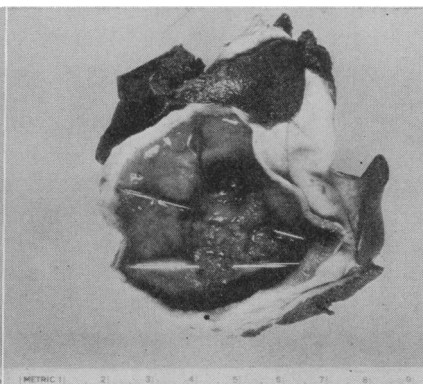


Fig. 7.—Primary adenocarcinoma in a pig's gall-bladder.

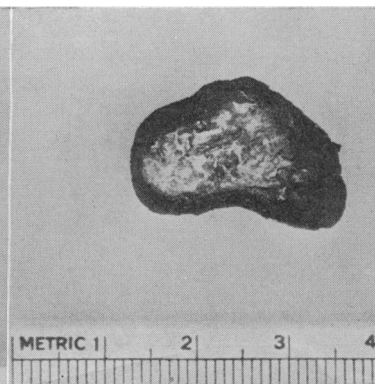


Fig. 8.—Stone incrustated polyp from a pig's gall-bladder.

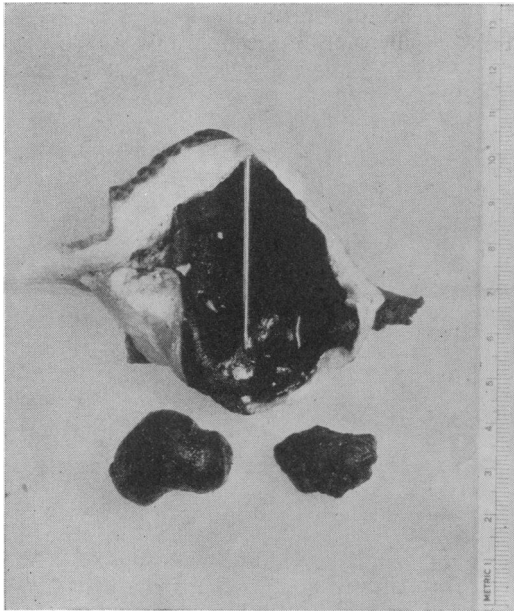


Fig. 9.—Gall-bladder and attached polyp with two cholesterol stones from a sow.

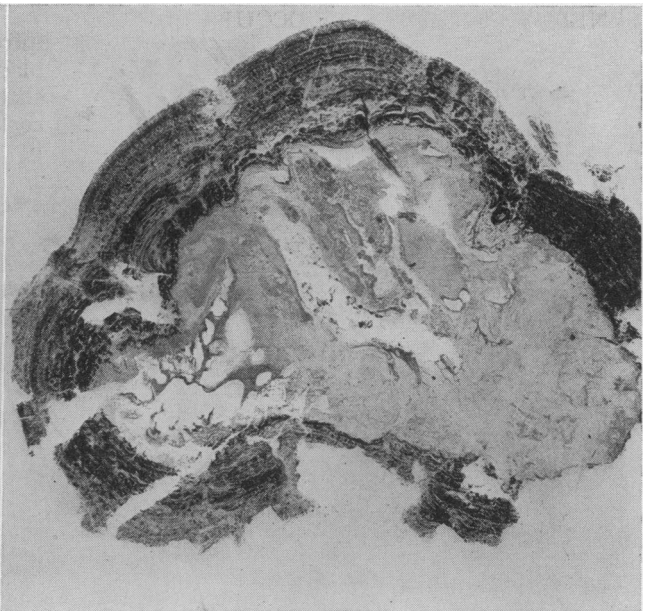


Fig. 10.—Sectioned stone showing polyp nucleus.

recovered from a pig. There were two distinct cystic ducts emptying into the common hepatic duct (Fig. 6). Another pig's gall-bladder showed a true congenital diverticulum. Two small diverticula were found in a cow's gall-bladder in which three large cholesterol stones were also recovered in the series of Gauss and Davis.

A well-localized, pedunculated, cauliflower-like adenocarcinoma was found in a pig's gall-bladder, arising from the ventral third of the gall-bladder wall. There were no stones or other pathology in this specimen. Microscopically the tumor was a typical primary adenocarcinoma of the gall-bladder; apparently growing slowly, and identical with similar specimens from man.

The most interesting specimen in this series was a large benign polyp, about which cholesterol material and bile pigments had precipitated to form a gall-stone (Fig. 8). The pedicle of the stone-encrusted polyp was attached to the gall-bladder wall and was partially coated with stone material. In addition, there were two cholesterol-rich stones, the size of a hazel nut, free in the gall-bladder cavity (Fig. 9). Microscopic sections of the stone show the polyp-like central nucleus with alternate laminations of pigment and cholesterol strata (Fig. 10). This is the best specimen I have seen illustrating the thesis that polyps or papillomata form the nuclei of some gall-stones. I have sectioned many gall-stones in which it has been possible to demonstrate the tissue structure of the nucleus, and I have twice before encountered pigment and cholesterol incrustations on polyps in the human gall-bladder, but this specimen contains the largest polypoid nucleus and the greatest amount of stone material that I have seen.

SUMMARY

1. Gall-stones were found in 0.72 per cent of 964 pigs' gall-bladders, and in 1.75 per cent of four hundred adult sheep's gall-bladders.

2. Only 60 per cent of the stones occurred in the swill-fed hogs, while 40 per cent were recovered from the gall-bladders of grain-fed hogs. However, cholesterol stones came entirely from swill-fed hogs, while bilirubin calcium stones were found in the grain-fed hogs.

3. One cholesterol stone was found in four hundred sheep's gall-bladders, while six cases had bilirubin calcium stones. None of one hundred lambs' gall-bladders had gall-stones.

4. Sex, and particularly pregnancy, were the factors of greatest importance in the incidence of gall-stones in pigs.

5. Cholesterosis was noted in 22.1 per cent of the pigs' gall-bladders and was found equally in the swill-fed and grain-fed hogs. Five instances were discovered among four hundred adult sheep's gall-bladders.

6. Pregnancy seemed to be the most important associated factor in cholesterosis.

7. Large lymph node-like structures were observed in 0.4 per cent of the pigs' gall-bladder walls. They are not normal areas, but their significance is not understood.

8. Acute or subacute cholecystitis occurred in 0.31 per cent of the pigs' gall-bladders—3.2 per cent of the sheep, and 1.2 per cent of the cattle.

9. Duplication of the gall-bladder, congenital diverticulum, primary adenocarcinoma, and incrustation of a benign polyp were incidental, but interesting lesions found in pigs' gall-bladders.

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REFERENCES

- Gauss, H., and Davis, C. L.: The Incidence of Gall-Stones in Cattle, *J. Am. Vet. Med. Assn.*, 81:71 (July), 1932.
- Totten, cited by Feldman, W. H.: Adenocarcinoma in the Gall-Bladder of a Cow. *Jour. Cancer Res.*, 12:188, 1929.
- Mentzer, S. H.: The Pathogenesis of Biliary Calculi, *Arch. Surg.*, 14:14, Part 1 (Jan.), 1927.